Practitioner's Docket No. **698.22-US1**

CHAPTER II

TRANSMITTAL LETTER TO THE UNITED STATES ELECTED OFFICE (EO/US)

(ENTRY INTO U.S. NATIONAL PHASE UNDER CHAPTER II)

PCT/GB00/00749	03 March 2000 (3.03.00)	05 March 1999 (5.03.99)
International Application Number	International Filing Date	International Earliest Priority Date

TITLE OF INVENTION: **Skin Wrinkle Reduction Using Pulsed Light**

APPLICANT(S): **ICN Photonics Limited; Michael Noel Kiernan; Robert Marc Clement**

Box PCT
Assistant Commissioner for Patents
Washington D.C. 20231
ATTENTION: EO/US

1. Applicant herewith submits to the United States Elected Office (EO/US) the following items under 35 U.S.C. Section 371:

   a. This express request to immediately begin national examination procedures (35 U.S.C. Section 371(f)).

   b. The U.S. National Fee (35 U.S.C. Section 371(c)(1)) and other fees (37 C.F.R. Section 1.492) as indicated below:

CERTIFICATION UNDER 37 C.F.R. SECTION 1.10*

I hereby certify that this paper, along with any document referred to, is being deposited with the United States Postal Service on this date 8/29/01, in an envelope as "Express Mail Post Office to Addressee," mailing Label Number **EL751090287US**, addressed to the: Assistant Commissioner for Patents, Washington, D.C. 20231.

Collene Houston

Collene Houston

2. Fees

CLAIMS FEE*	(1) FOR	(2) NUMBER FILED	(3) NUMBER EXTRA	(4) RATE	(5) CALC-ULATIONS
	TOTAL CLAIMS	31 -20 =	11	x $18.00 =	$198.00
	INDEPEN-DENT CLAIMS	3 - 3 =	0	x $80.00 =	$0.00
	MULTIPLE DEPENDENT CLAIM(S) (if applicable) + $270.00				$0.00
BASIC FEE	U.S. PTO WAS NOT INTERNATIONAL PRELIMINARY EXAMINATION AUTHORITY Where no international preliminary examination fee as set forth in Section 1.482 has been paid to the U.S. PTO, and payment of an international search fee as set forth in Section 1.445(a)(2) to the U.S. PTO has not been paid (37 C.F.R. Section 1.492(a)(3)) $1,000.00				$1,000.00
	Total of above Calculations				$1,198.00
SMALL ENTITY	Reduction by 1/2 for filing by small entity, if applicable.				- $599.00
	Subtotal				$599.00
	Total National Fee				$599.00
	Fee for recording the enclosed assignment document $40.00 (37 C.F.R. Section 1.21(h)). See attached "ASSIGNMENT COVER SHEET".				$0.00
TOTAL	Total Fees enclosed				$599.00

*See attached Preliminary Amendment Reducing the Number of Claims.

A check in the amount of $599.00 to cover the above fees is enclosed.

3. A copy of the International application as filed (35 U.S.C. Section 371(c)(2)) has been transmitted by the International Bureau. Form PCT/IB/308 is attached.

Date of mailing of the application (from form PCT/IB/308): 14 September 2000

4. A translation of the International application into the English language (35 U.S.C. Section 371(c)(2)) is not required as the application was filed in English.

5. Amendments to the claims of the International application under PCT Article 19 (35 U.S.C. Section 371(c)(3)) have not been transmitted. Applicant chose not to make amendments under PCT Article 19.

Date of mailing of Search Report (from form PCT/ISA/210): 29 June 2000.

6. A translation of the amendments to the claims under PCT Article 19 (38 U.S.C. Section 371(c)(3)) has not been transmitted for reasons indicated in section 5.

7. A copy of the international examination report (PCT/IPEA/409) is transmitted herewith.

8. Annex(es) to the international preliminary examination report is/are transmitted herewith.

9. A translation of the annexes to the international preliminary examination report is not required as the annexes are in the English language.

10. An oath or declaration of the inventor (35 U.S.C. Section 371(c)(4)) complying with 35 U.S.C. Section 115 will follow.

11. An International Search Report (PCT/ISA/210) or Declaration under PCT Article 17(2)(a) is transmitted herewith.

12. An Information Disclosure Statement under 37 C.F.R. Sections 1.97 and 1.98 will be transmitted within THREE MONTHS of the date of submission of requirements under 35 U.S.C. Section 371(c).

13. Additional documents:

a. International Publication No. WO00/53114

Specification, claims and drawing

b. Preliminary amendment (37 C.F.R. Section 1.121)

c. Notification Concerning Submission of Priority Document (Form PCT/IB/304)

14. The above items are being transmitted before 30 months from any claimed priority date.

AUTHORIZATION TO CHARGE ADDITIONAL FEES

The Commissioner is hereby authorized to charge the following additional fees that may be required by this paper and during the entire pendency of this application to Account No.: 500341

37 C.F.R. Section 1.492(a)(1), (2), (3), and (4) (filing fees)
37 C.F.R. Section 1.492(b), (c), and (d) (presentation of extra claims)
37 C.F.R. Section 1.17 (application processing fees)
37 C.F.R. Section 1.17(a)(1)-(5) (extension fees pursuant to Section 1.136(a))

Date: 8/28/01

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

WASHINGTON, D.C. 20231

Inventor: **Clement et al.**	Examiner: **Not yet assigned**
Serial No: **Not yet assigned**	Art Unit: **Not yet assigned**
Filed: **August 28, 2001**	
For: **Skin Wrinkle Reduction Using Pulsed Light**	

PRELIMINARY AMENDMENT

The Honorable Commissioner
of Patents and Trademarks
Washington, D.C. 20231

Dear Sir:

This preliminary amendment is being filed concurrently with a US National Phase (371) of International Application PCT/GB00/00749. Please enter the following:

IN THE SPECIFICATION

Please amend the specification by inserting the following sentence at the beginning of the specification: This application is a national phase (371) application based on international application no. PCT/GB00/00749, filed on March 3, 2000, which claims priority to British application no. GB 9905173.2, filed on March 5, 1999, which corresponds to US application no. 09/263422, also filed on March 5, 1999, which is incorporated herein by reference and to which this application claims a benefit as well.

IN THE CLAIMS

1. (Amended) An apparatus for cosmetic reduction of wrinkles on a superficial area of mammalian skin, the apparatus comprising a radiation delivery system for delivering electromagnetic radiation of a light wavelength to the skin, the radiation delivery system including a pulsation system for pulsing the radiation delivered according to a predetermined regime, the apparatus being intended to be configured such that the radiation delivered to the

skin is of a predetermined monochromatic wavelength or a narrow wavelength bandwidth substantially in the range of 500nm-850nm and pulse energy rise time substantially at or below 200μs.

2. (Amended) The apparatus according to claim 1, wherein the pulse energy rise time is substantially in the range of 50μs to 150μs.

3. (Amended) The apparatus according to claim 1 [or claim 2], wherein the radiation energy density delivered to the skin is substantially at or below 5J/cm^2 per pulse.

4. (Amended) The apparatus according to claim 1 [any preceding claim], wherein the energy pulse duration is substantially at or below 100ms.

5. (Amended) The apparatus according to claim 4, wherein the energy pulse duration is substantially at or below 2ms.

6. (Amended) The apparatus according to claim 5, wherein the energy pulse duration is substantially at or below 200μs.

7. (Amended) An apparatus for cosmetic reduction of wrinkles on superficial mammalian skin, the apparatus comprising a radiation delivery system for delivering substantially monochromatic radiation, said radiation being in a wavelength bandwidth of substantially 15nm or less and in at least one of the ranges of 570nm to 600nm and 750nm to 850nm, the delivery system including a pulsation system for pulsing the radiation delivered according to a predetermined regime in which the radiation delivered to the skin has an energy density substantially at or below [to] 5J/cm^2 per pulse.

8. (Amended) The apparatus according to claim 7 [any preceding claim], wherein the radiation delivery system is set up to deliver substantially monochromatic radiation in a bandwidth of substantially 15nm or less substantially in at least one of the ranges of 577nm to 585nm and 800nm to 815nm.

9. (Amended) The apparatus according to claim 7 [any preceding claim], wherein the

radiation delivery system is set up to deliver radiation in a concentrated beam having a cross section with a substantially uniform energy distribution across said beam cross section.

10. (Amended) The apparatus according to claim 7 [any preceding claim], wherein the radiation delivery system is set up to deliver radiation in a concentrated beam having a diameter substantially in the range of 1mm to 10mm.

11. (Amended) The apparatus according to claim 7 [any preceding claim], wherein the radiation delivery system comprises a laser radiation delivery system.

12. (Amended) The apparatus according to claim 11, wherein the laser radiation delivery system comprises a dye laser radiation delivery system.

13. (Amended) The apparatus according to claim 12, wherein the dye laser radiation delivery system comprises a flashlamp pumped dye laser including a pulse forming network arranged to pulse the laser according to the predetermined pulse regime.

14. (Amended) The apparatus according to claim 11, wherein the laser radiation delivery system comprises a semiconductor laser radiation delivery system.

15. (Amended) The apparatus according to claim 1 or claim 7 [any of claims 1 to 11], wherein the radiation delivery means includes a broad band radiation emitting device.

16. (Amended) The apparatus according to claim 12, wherein the radiation delivery means includes at least one radiation filter arranged to filter radiation to permit the substantially monochromatic (or narrowed bandwidth) radiation to be delivered to the skin.

17. (Amended) The apparatus according to claim1 or claim 7 [any preceding claim], further comprising a control system arranged to permit the energy density to be varied within the range of $0.5J/cm^2$ and $5J/cm^2$.

18. (Amended) The apparatus according to claim 17, wherein the control means is arranged

to inhibit selection of an energy density substantially above 5J/cm^2.

19. (Amended) The apparatus according to claim1 or claim 7 [any preceding claim], which includes an optical arrangement for focusing the radiation beam.

26. (Amended) A method according to [according to any of claims 20 to 25] claim 20, wherein the pulse energy rise time is substantially in the range of 50μs to 150μs.

27. (Amended) A method according to [any of claims 20 to 25] claim 20, wherein the energy pulse duration is substantially at or below 100ms.

REMARKS

The amendments herein to do not constitute any new matter.

Respectfully submitted,
Fish & Associates

Dated: August 28, 2001

By: _____
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CLEAN SET OF CLAIMS AS AMENDED ON 8/28/01

1. An apparatus for cosmetic reduction of wrinkles on a superficial area of mammalian skin, the apparatus comprising a radiation delivery system for delivering electromagnetic radiation of a light wavelength to the skin, the radiation delivery system including a pulsation system for pulsing the radiation delivered according to a predetermined regime, the apparatus being intended to be configured such that the radiation delivered to the skin is of a predetermined monochromatic wavelength or a narrow wavelength bandwidth substantially in the range of 500nm-850nm and pulse energy rise time substantially at or below 200μs.

2. The apparatus according to claim 1, wherein the pulse energy rise time is substantially in the range of 50μs to 150μs.

3. The apparatus according to claim 1 wherein the radiation energy density delivered to the skin is substantially at or below 5J/cm^2 per pulse.

4. The apparatus according to claim 1, wherein the energy pulse duration is substantially at or below 100ms.

5. The apparatus according to claim 4, wherein the energy pulse duration is substantially at or below 2ms.

6. The apparatus according to claim 5, wherein the energy pulse duration is substantially at or below 200μs.

7. An apparatus for cosmetic reduction of wrinkles on superficial mammalian skin, the apparatus comprising a radiation delivery system for delivering substantially monochromatic radiation, said radiation being in a wavelength bandwidth of substantially 15nm or less and in at least one of the ranges of 570nm to 600nm and 750nm to 850nm, the delivery system including a pulsation system for pulsing the radiation delivered according to a predetermined regime in which the radiation delivered to the skin has an energy density substantially at or below 5J/cm^2 per pulse.

8. The apparatus according to claim 7, wherein the radiation delivery system is set up to deliver substantially monochromatic radiation in a bandwidth of substantially 15nm or less substantially in at least one of the ranges of 577nm to 585nm and 800nm to 815nm.

9. The apparatus according to claim 7, wherein the radiation delivery system is set up to deliver radiation in a concentrated beam having a cross section with a substantially uniform energy distribution across said beam cross section.

10. The apparatus according to claim, wherein the radiation delivery system is set up to deliver radiation in a concentrated beam having a diameter substantially in the range of 1mm to 10mm.

11. The apparatus according to claim 7, wherein the radiation delivery system comprises a laser radiation delivery system.

12. The apparatus according to claim 11, wherein the laser radiation delivery system comprises a dye laser radiation delivery system.

13. The apparatus according to claim 12, wherein the dye laser radiation delivery system comprises a flashlamp pumped dye laser including a pulse forming network arranged to pulse the laser according to the predetermined pulse regime.

14. The apparatus according to claim 11, wherein the laser radiation delivery system comprises a semiconductor laser radiation delivery system.

15. The apparatus according to claim 1 or claim 7, wherein the radiation delivery means includes a broad band radiation emitting device.

16. The apparatus according to claim 12, wherein the radiation delivery means includes at least one radiation filter arranged to filter radiation to permit the substantially monochromatic (or narrowed bandwidth) radiation to be delivered to the skin.

17. The apparatus according to claim1 or claim 7, further comprising a control system arranged to permit the energy density to be varied within the range of 0.5J/cm^2 and 5J/cm^2.

18. The apparatus according to claim 17, wherein the control means is arranged to inhibit selection of an energy density substantially above $5J/cm^2$.

19. The apparatus according to claim1 or claim 7, which includes an optical arrangement for focusing the radiation beam.

20. A method of cosmetically reducing wrinkles from a superficial area of mammalian skin tissue having, in the order specified, an epidermal layer, a basal layer, and a dermal layer, which method comprises irradiating said dermal layer through said basal layer by means of visible or infra-red radiation, said irradiation being selected to be absorbed by a chromophore in targeted capillaries present in said dermal layer, the targeted capillaries having fenestrations permitting transfer of inflammatory mediators through the capillary wall upon selective heating to a threshold level, while said basal layer remains intact so as to substantially inhibit contact of said dermal layer with ambient air, said irradiation being pulsed and having:

    i) an energy density of substantially $5J/cm^2$ or less; and/or,

    ii) energy pulse rise time substantially at or below 200μs.

21. A method according to claim 20, wherein the irradiation is from a substantially monochromatic radiation source in a bandwidth of substantially 15nm or less.

22. A method according to claim 21, wherein said irradiation is from a coherent radiation source.

23. A method according to claim 22, wherein the source comprises a ruby laser arranged to target the dermis.

24. A method according to claim 22, wherein the source comprises a dye laser of wavelength selected to target oxyhemoglobin present in blood vessels in said dermal layer.

25. A method according to claim 22, wherein the source comprises a dye laser, a ruby laser, or a semiconductor laser which scans said area of mammalian skin tissue.

26. A method according to claim 20, wherein the pulse energy rise time is substantially in the range of 50μs to 150μs.

27. A method according to claim 20, wherein the energy pulse duration is substantially at or below 100ms.

28. A method according to claim 27, wherein the energy pulse duration is substantially at or below 2ms.

29. A method according to claim 28, wherein the energy pulse duration is substantially at or below 2μs.

30. A method according to claim 20, in which said superficial area of mammalian skin tissue is treated with an artificial chromophore which is absorbed into the dermal layer.

31. A method according to claim 30, wherein the artificial chromophore is applied to the epidermal layer in the form of a liposome-containing topical formulation.

SKIN WRINKLE REDUCTION USING PULSED LIGHT

The present invention relates to a method of reducing wrinkles from a superficial area of mammalian skin tissue, and apparatus therefor.

The application of laser technology in healthcare is well known, and the use of lasers in medical applications has been studied extensively since the early 1960's. In recent years an increasing interest has been shown in cosmetic applications. Two such cosmetic applications are skin resurfacing and wrinkle removal; in this field lasers can be used as an alternative to surgical facelifts.

There is a distinct difference between wrinkle removal and skin resurfacing. Skin resurfacing is where laser energy vaporizes thin layers of the epidermis without breaking through the basal layer into the dermis. This is essentially a superficial process primarily used to give the skin a "fresher" appearance. However, wrinkle removal as a more aggressive technique where tissue is removed layer by layer, invading the dermis and effectively inducing a second degree burn. Heat is deposited in the dermis shrinking the collagen and tightening the skin.

In young skin, the collagen just beneath the surface of the skin forms an organized lattice with good elasticity and flexibility. During aging, the collagen changes its structure impacting negatively on the cosmetic appearance

of the skin. Several techniques have been developed to induce a "controlled injury" to the dermis in an attempt to generate rejuvenation of the collagen structure returning the skin to an earlier cosmetic appearance. During the 1990's a laser approach to wrinkle removal has been introduced.

For known wrinkle removal techniques, the wavelength is chosen so that the laser energy is highly absorbed in water, the current lasers of choice being the CO_2 laser at 10.6μm wavelength and the Erbium YAG laser at 2.94μm wavelength. In this non-selective process, pulses of laser energy are applied to the skin surface, each pulse vaporizing a layer of tissue between 30μm to 60μm in thickness. Normally, the first pass of the laser removes a thin layer of the epidermis without damaging the basal layer. Successive passes over the same area penetrate into the dermis and heat the collagen. The laser operator sees this thermal build-up "shrink" the skin in "real time", tightening up the skin's appearance. When the desired clinical outcome is achieved, the operator ceases applying laser pulses. It is therefore apparent that the quality of the cosmetic result is highly dependent upon the experience and skill of the operator.

In the case of CO_2 laser wrinkle removal, post-treatment supervision of the patient is a necessity. Immediately after treatment, the skin is essentially an open wound requiring dressings in place for 2-10 days. Additionally, topically applied lotions are required for patient comfort and prevention of infection. Post-operative infection is

common, primarily due to removal of the natural protective barrier of the skin, with a reported incidence of between 4.5 to 7%.

On average, with CO_2 laser wrinkle removal, post-treatment erythema is present for 4-5 months. This compares to 2-3 months following a Chemical Peel. Also, the incidence of side effects is significant, the most common being hyperpigmentation occurring in 30-40% of cases. Higher incidences are reported in darker skin types. A delayed hypopigmentation, which can occur up to a year after the procedure was performed, has recently emerged as a complication of aggressive laser resurfacing. Many of the eminent laser resurfacing surgeons have resorted to less aggressive techniques.

The effect of known procedures is two fold:

(a) the laser induces denaturing of the collagen in the dermis, and the formation of cross links, which results in a tightening effect stretching the skin, reducing or removing the wrinkles (it is thought that the thermal threshold for this effect is a temperature of 70°C); and

(b) the changes to the dermis induce the generation of new collagen which develops using the matrix created by the denatured collagen as a foundation.

The skin-resurfacing and wrinkle removal procedure outlined above is considered by many experts in the field

as a significant improvement over previously used surgical methods. The procedure uses the laser's ability to deliver high energy density at the surface of tissue and hence ablate the surface tissue in a well controlled manner. Continuing to remove the tissue, layer by layer is designed to damage the collagen and hence induce wrinkle removal. This second stage of the procedure is primitive; the skin weeps, scabs form and redness of the skin appears for many weeks.

It is therefore the primary object of the present invention to provide a technique for removing wrinkles from a superficial area of mammalian skin tissue without causing secondary burns and other problems associated with traditional wrinkle removal.

The present invention provides a method of removing wrinkles from a superficial area of mammalian skin tissue. The dermal layer of the tissue is irradiated through the basal layer by radiation selected to be absorbed by a chromophore in the dermal layer such that collagen present in the dermal layer is heated, while the basal layer remains intact so as to substantially inhibit contact of the dermal layer with ambient air.

A particular advance of the present invention relies on the specific targeting of smaller capillaries, typically of a diameter in the 15-20μm range located in the upper dermis. These smaller capillaries have fenestrations which permit transfer of inflammatory mediators from the vessel through the vessel wall structure without causing

injury to the tissue or vessel. Selective targeting of these vessels and minimisation of interaction with other tissue components results in significant enhancement of the process.

According to an important feature of the present invention the wavelength of the stimulating electromagnetic radiation is selected to be substantially in the range 500nm-850nm (more preferably 500-600nm) and the stimulating electromagnetic radiation is pulsed to have a rise time substantially at or below 200μs (preferably substantially in the range 1μs to 150μs, more preferably substantially in the range 5μs to 150μs).

The wavelength range specifically targets the capillaries, the primary chromophore being oxyhaemoglobin.

The rapid rise time of the energy delivered in a pulse is important because, for vessels in the quoted size range, the thermal relaxation time is short (typically of the order of 100μs to 200μs). This signifies that heat is lost from the targeted vessels at a rapid rate; it is therefore important to ensure that energy is delivered rapidly enough to stimulate migration of the required inflammatory mediators, whilst compensating for the heat lost during the energy pulse. Typically an energy pulse rise time in the order of 50μs to 150μs, with a pulse duration up to 100ms (more preferably up to 2ms) is adequate although lower pulse durations in the range of up to 200μs may be sufficient and preferable.

The radiation delivery system beneficially delivers a radiation beam of predetermined monochromatic wavelength or narrow wavelength bandwidth to the skin.

The total radiation energy density delivered to the skin is preferably substantially at or below 5J/cm^2 per pulse (preferably substantially in the range 0.5J/cm^2 to 5J/cm^2 per pulse).

An artificial chromophore may be introduced into the desired area for wrinkle reduction, or a naturally occurring chromophore may be selected. In a preferred embodiment of the technique, the naturally occurring chromophore selected is oxyhemoglobin of the dermal plexus which has wavelength absorbtion peaks at 585nm and 815nm, at which wavelengths absorbtion in surrounding tissue components is relatively low.

According to a further aspect, the invention therefore provides apparatus for cosmetic reduction of wrinkles on a superficial area of mammalian skin, the apparatus comprising a radiation delivery system for delivering substantially monochromatic radiation in a bandwidth of substantially 15 nm or less in at least one of the ranges 570nm to 600nm and 750nm to 850nm, the delivery system including a pulsation system for pulsing the radiation delivered according to a predetermined regime in which the rise time of the energy pulse is substantially at or below 200μs (preferably substantially in the range 1μs to 150μs, more preferably substantially in the range 5μs to 150μs).

The energy density of the substantially monochromatic radiation in the bandwidth of substantially 15nm or less delivered to the skin is preferably substantially at or below 5J/cm^2 per pulse.

The method according to the invention is non-invasive and non-ablative and can readily be performed by non-medical personnel. The total energy delivered per pulse is sufficient to effect the required physical change in the tissue surrounding the target chromophore without causing ablation of the target or other skin components through which the radiation passes.

The radiation is preferably substantially monochromatic or at least of a relatively narrow wavelength bandwidth to ensure that it is preferentially selectively absorbed by the target chromophore. A laser source may be used to produce the required wavelength, or a filtered broad band light source, such as an LED may be used with appropriate filtering to permit the selected wavelength (or narrow wavelength band) to pass.

The irradiation may be by means of a source of visible or infra-red radiation (suitably filtered to remove deleterious ultra-violet radiation if necessary). The radiation may be coherent (that is from a laser source). Such a laser source may be, for example, a dye laser, a ruby laser, or a semiconductor laser. If a dye laser is used, its wavelength is preferably such that it is absorbed by oxyhemoglobin (as naturally occurring chromophore present in blood vessels in the dermis).

Alternatively, the superficial area may be treated with an artificial chromophore which is absorbed into the dermal layer. Such an artificial chromophore may be applied to the epidermal layer in the form of a liposome-containing topical formulation. The chromophore may then permeate through the basal layer for delivery to the dermal layer.

When a laser is used, it may be arranged to scan the superficial area and/or to irradiate the dermal layer in pulses. When the laser is in pulsed mode, the pulses typically have duration of 10μsec to 10msec (more preferably 200μsec to 1msec).

It is sometimes desirable to remove part of the epidermis prior to irradiating the dermal layer according to the invention. Such epidermis removal (known as skin resurfacing) may be effected mechanically (for example by abrasion), or by means of laser radiation. When laser radiation is used for this purpose, it is typically a scanner controlled CO_2 laser source.

The energy density per pulse is preferably accurately controlled to ensure that a maximum threshold level (substantially of 5J/cm^2) is not exceeded.

The invention will now be further described in specific embodiments, by way of example only and with reference to the accompanying drawings, in which:

Figure 1 is a schematic representation of the three outermost layers of mammalian skin tissue;

Figure 2 is a schematic representation of partial removal of the epidermis (skin resurfacing), which is an optional step according to the invention;

Figure 3 is a schematic illustration of the result of a prior art method of wrinkle removal, which is surgical because it involves full removal of the epidermis in a selected area and therefore exposure of the dermis and consequent second degree burning;

Figure 4 is a schematic illustration of the result of the method according to the invention, showing that the epidermis is partially intact and the basal layer fully intact;

Figure 5, is a schematic diagram of a first embodiment of wrinkle reduction apparatus according to the invention;

Figure 6 is a schematic diagram of an alternate embodiment of wrinkle reduction apparatus according to the invention;

Figure 7 is a schematic representation of an optical delivery system forming part of apparatus according to the invention; and,

Figure 8 is a graphical representation showing the intensity profile of the radiation delivered using apparatus according to the invention.

Referring to Figure 1, the basic skin structure of mammalian skin tissue comprises three layers, the outermost epidermis 1 which is adjacent to the basal layer 2 and then the dermis 3.

Referring to Figure 2, partial removal of an area 4 of epidermis 1 by means of CO_2 laser radiation is known as skin resurfacing. This stage represents the first step of a prior art method but is an optional step according to the invention. Both the basal layer 2 and the dermis 3 are unaffected by the laser radiation.

As shown in Figure 3, prior art method of wrinkle removal results in complete removal of an area 5 of epidermis 1 and basal layer 2 by repeated exposure to CO_2 laser radiation. Partial removal of the dermis 3 also occurs, as represented by 6, leaving the dermis exposed to air. This causes a second degree burn which is slow to heal and a risk of infection.

As shown in Figure 4, the method of wrinkle removal according to the invention results in partial removal of the epidermis 1 (this is an optional step as described in Figure 2 above) and the basal layer 2 is left intact, such that the dermis 3 is not exposed to air. Laser radiation 7 is applied to the tissue and selectively absorbed by a chromophore in the dermis 3, heating the collagen and shrinking the skin hence removing the appearance of wrinkles.

In a preferred embodiment, the target chromophore selected

is oxyhemoglobin in the dermis 3 which has absorbtion peaks at approximately 585nm and 815nm. The apparatus shown in Figure 5 comprises a laser radiation delivery system 101 comprising a flashlamp excited pumped dye laser including a laser head 102, dye reservoir 103 and pump 104. A flowmeter 105 regulates dye flow to the laser cavity in the laser head 102 and a cooling system 106 cools the laser head 102 and dye reservoir 103. The system is controlled by a microprocessor controller 107 which operates voltage control of a pulse forming network 108 (including a capacitor and inductor network) which initiates a discharge pulse and consequently a pulsed beam laser output from laser head 102. Voltage control and feedback is provided between the microprocessor controller 107 and pulse forming network 108 via link 109. Temperature monitoring feedback is provided between the cooling system and the controller 107 via link 110.

The system parameters and laser head operates to output controlled pulses of laser radiation having wavelength in the range 577nm to 585nm and a pulse duration typically in the range 200μs to 1ms. In view of the need to selectively target small capillaries in the dermis, the energy pulse rise time is accurately controlled to be sufficiently rapid to produce the desired selective heating effect (as described earlier in the specification). The energy pulse rise time is substantially at or below 150ms. To produce the required wavelength an appropriate laser dye is selected (such as Rhodamine 575 or Pyromethene 590), the concentration of the dye solution is controlled.

Control of the pulse duration for the dye laser arrangement 101 is achieved by accurate control of the energy delivered to the exciting flashlamps in the laser head 102 by tailoring the capacitor and inductor values in the pulse forming network 108.

The energy is delivered to the skin surface via a fiberoptic tube 112 (see Figure 7) and a focussing optical lens arrangement 113 which is configured to focus a light spot onto the skin tissue surface so as to have a spot diameter within the range 1mm to 10mm, and an intensity distribution across the spot diameter that is substantially uniform (i.e. "a top hat" distribution), as shown in Figure 8 having the required rapid rise time at or below 150ms. Providing optics to ensure that the uniform energy distribution results in even heating of the tissue without the occurrence of "hot spots" which could result in tissue damage/oblation.

The radiation parameters are also selected to ensure that the total radiation energy density delivered per pulse falls substantially within the range 0.5J/cm^2 to 5J/cm^2. It is particularly important that the selected upper threshold value (5J/cm^2) is not exceeded significantly as delivery of a higher energy densities of radiation per pulse can result in unwanted effects on the skin (such as ablation and/or other damage).

For the dye laser system 101 of Figure 1, the energy density of the radiation delivered to the skin is controlled by adjustment of the flashlamp output energy

(which in turn controls the laser output energy). The laser output energy in conjunction with the spot site determines the energy density delivered. Accurate control is achieved by control of the dye circulation rate, the dye temperature and the flashlamp output energy. Dye circulation rate is important because repeated pulsing of the same volume of dye, without circulation, reduces the output energy of the laser head 102. Increasing or decreasing the dye temperature has an affect on the energy output of the laser head 102. The flashlamp output energy is controlled by varying the voltage with which the capacitors in the pulse forming network 108 are charged; feedback of the capacitor voltage via link 109 is therefore important.

The energy density required will vary within the specified range from person to person, depending upon skin colour.

Referring to Figure 6, there is shown an alternative embodiment of apparatus for performance of the invention in which an LED or semiconductor laser device 202 may be utilised to produce the output radiation 220. A user interface 213 enables input into a microprocessor controller 207 which is used to control a power supply unit 214 to ensure that the required current is supplied to the LED or semiconductor laser device 220. A temperature sensor 215 provides temperature feedback via a link 210. Output 216 from controller 207 sets the current supplied by the power supply unit 214 to the device 202; input 217 into the controller 207 provides current monitoring feedback. Control of the pulse

duration is achieved by pulsing the current supply from power supply unit 214 to the LED or semiconductor laser device 202.

High intensity LED devices are capable of producing wavelengths corresponding to the 585nm absorption peak of oxyhaemoglobin. The optical system (including lens 113) may include filters arranged to narrow the band of radiation passing from the LED to the target area of the skin. Where lasers are used, the output may be monochromatic. Alternatively, or in the case where LED's are used, the radiation delivered may be "effectively" monochromatic, or of a relatively narrow band width (typically within a band width of 15nm or less).

Where a semiconductor laser device is used, the output may correspond to the second (higher) absorption peak (815nm) for oxyhaemoglobin.

Whilst the invention has been described in relation to delivery of effectively monochromatic radiation (or within specific narrow band widths) at one or other of the oxyhaemoglobin absorption peaks of 585nm and 815nm, it is clear that the beneficial effect of the invention can be achieved to a certain degree by using wavelengths relatively close to, but either side, of the respective absorption peaks. Preferred wavelength ranges for operation are 570nm to 600nm and 750nm to 850nm for targeting oxyhaemoglobin.

Where an artificial chromophore is used, the wavelength (or narrow band of wavelengths) is selected to correspond to a characteristic absorption wavelength of the relevant chromophore. It remains important to ensure that the total energy delivered per pulse is below the threshold damage level (approximately $5J/cm^2$).

In the embodiments described, it is important to ensure that there is not excess energy (and therefore heat) build-up in the target, and therefore the inter pulse duration is selected at a level to avoid this situation occurring. It is preferred that the pulse repetition rate is substantially in the range 3Hz maximum or less.

Claims:

1. Apparatus for cosmetic reduction of wrinkles on a superficial area of mammalian skin, the apparatus comprising a radiation delivery system for delivering electromagnetic radiation of light wavelength to the skin, the radiation delivery system including a pulsation system for pulsing the radiation delivered according to a predetermined regime, the apparatus being intended to be configured such that the radiation delivered the skin is of predetermined monochromatic wavelength or narrow wavelength bandwidth substantially in the range 500nm-850nm and pulse energy rise time substantially at or below 200μs.

2. Apparatus according to claim 1, wherein the pulse energy rise time substantially in the range 50μs to 150μs.

3. Apparatus according to claim 1 or claim 2, wherein the radiation energy density delivered to the skin substantially at or below 5J/cm^2 per pulse.

4. Apparatus according to any preceding claim, wherein the energy pulse duration is substantially at or below 100ms.

5. Apparatus according to claim 4, wherein the energy pulse duration is substantially at or below 2ms.

6. Apparatus according to claim 5, wherein the energy pulse duration is substantially at or below 200μs.

7. Apparatus for cosmetic reduction of wrinkles on superficial mammalian skin, the apparatus comprising a radiation delivery system for delivering substantially monochromatic radiation, said radiation being in a wavelength bandwidth of substantially 15nm or less and in at least one of the ranges 570nm to 600nm and 750nm to 850nm, the delivery system including a pulsation system for pulsing the radiation delivered according to a predetermined regime in which the radiation delivered to the skin has an energy density substantially at or below to 5J/cm^2 per pulse.

8. Apparatus according to any preceding claim, wherein the radiation delivery system is set up to deliver substantially monochromatic radiation in a bandwidth of substantially 15nm or less substantially in at least one of the ranges 577nm to 585nm and 800nm to 815nm.

9. Apparatus according to any preceding claim, wherein the radiation delivery system is set up to deliver radiation in a concentrated beam having a cross-section with a substantially uniform energy distribution across said beam cross section.

10. Apparatus according to any preceding claim, wherein

the radiation delivery system is set up to deliver radiation in a concentrated beam having a diameter substantially in the range 1mm to 10mm.

11. Apparatus according to any preceding claim, wherein the radiation delivery system comprises a laser radiation delivery system.

12. Apparatus according to claim 11, wherein the laser radiation delivery system comprises a dye laser radiation delivery system.

13. Apparatus according to claim 12, wherein the dye laser radiation delivery system comprises a flashlamp pumped dye laser including a pulse forming network arranged to pulse the laser according to the predetermined pulse regime.

14. Apparatus according to claim 11, wherein the laser radiation delivery system comprises a semiconductor laser radiation delivery system.

15. Apparatus according to any of claims 1 to 11, wherein the radiation delivery means includes a broad band radiation emitting device.

16. Apparatus according to claim 12, wherein the radiation delivery means includes at least one radiation filter arranged to filter radiation to permit the substantially monochromatic (or narrowed bandwidth) radiation to be delivered to the skin.

17. Apparatus according to any preceding claim, further comprising a control system arranged to permit the energy density to be varied within the range 0.5J/cm^2 and 5J/cm^2.

18. Apparatus according to claim 17, wherein the control means is arranged to inhibit selection of an energy density substantially above 5J/cm^2.

19. Apparatus according to any preceding claim, which includes an optical arrangement for focussing the radiation beam.

20. A method of cosmetically reducing wrinkles from a superficial area of mammalian skin tissue having, in the order specified, an epidermal layer, a basal layer, and a dermal layer, which method comprises irradiating said dermal layer through said basal layer by means of visible or infra-red radiation, said irradiation being selected to be absorbed by a chromophore in targeted capillaries present in said dermal layer, the targeted capillaries having fenestrations permitting transfer of inflammatory mediators through the capillary wall upon selective heating to a threshold level, while said basal layer remains intact so as to substantially inhibit contact of said dermal layer with ambient air, said irradiation being pulsed and having:

i) an energy density of substantially 5J/cm^2

or less; and/or,

ii) energy pulse rise time substantially at or below 200μs.

21. A method according to claim 20, wherein the irradiation is from a substantially monochromatic radiation source in a bandwidth of substantially 15nm or less.

22. A method according to claim 21, wherein said irradiation is from a coherent radiation source.

23. A method according to claim 22, wherein the source comprises a ruby laser arranged to target the dermis.

24. A method according to claim 22, wherein the source comprises a dye laser of wavelength selected to target oxyhemoglobin present in blood vessels in said dermal layer.

25. A method according to claim 22, wherein the source comprises a dye laser, a ruby laser, or a semiconductor laser which scans said area of mammalian skin tissue.

26. A method according to according to any of claims 20 to 25, wherein the pulse energy rise time substantially in the range 50μs to 150μs.

27. A method according to any of claims 20 to 26, wherein the energy pulse duration is substantially at or below 100ms.

28. A method according to claim 27, wherein the energy pulse duration is substantially at or below 2ms.

29. A method according to claim 28, wherein the energy pulse duration is substantially at or below 200μs.

30. A method according to claim 20, in which said superficial area of mammalian skin tissue is treated with an artificial chromophore which is absorbed into the dermal layer.

31. A method according to claim 30, wherein the artificial chromophore is applied to the epidermal layer in the form of a liposome-containing topical formulation.

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 :
A61B 18/20

A1

(11) International Publication Number: WO 00/53114

(43) International Publication Date: 14 September 2000 (14.09.00)

(21) International Application Number: PCT/GB00/00749

(22) International Filing Date: 3 March 2000 (03.03.00)

(30) Priority Data:
9905173.2 5 March 1999 (05.03.99) GB

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(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: SKIN WRINKLE REDUCTION USING PULSED LIGHT

(57) Abstract

Wrinkles are cosmetically removed from a superficial area of mammalian skin tissue having an epidermal layer, a basal layer, and a dermal layer, by irradiating the dermal layer through the basal layer, the irradiation having an energy density in the range 5J/cm^2 or less, and being selected to be absorbed by a chromophore in the dermal layer such that collagen present in the dermal layer is heated, while the basal layer remains intact so as to substantially inhibit contact of the dermal layer with ambient air.

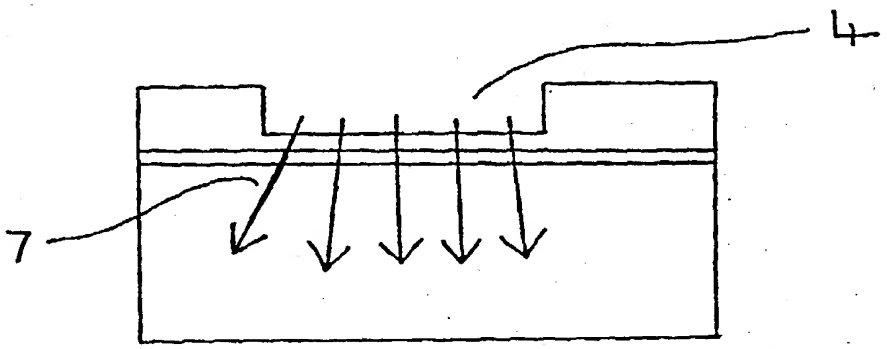
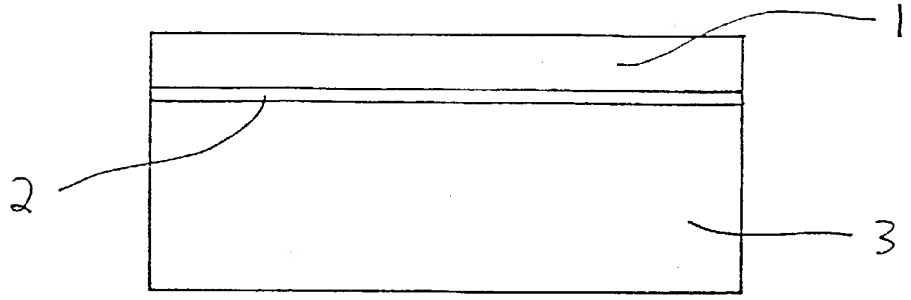


FIGURE 1



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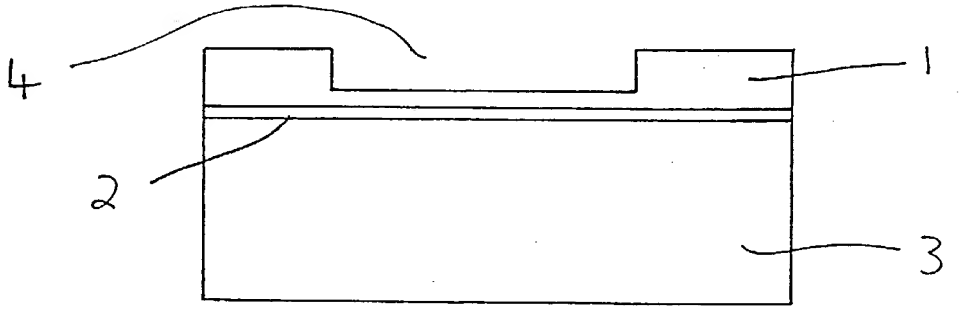

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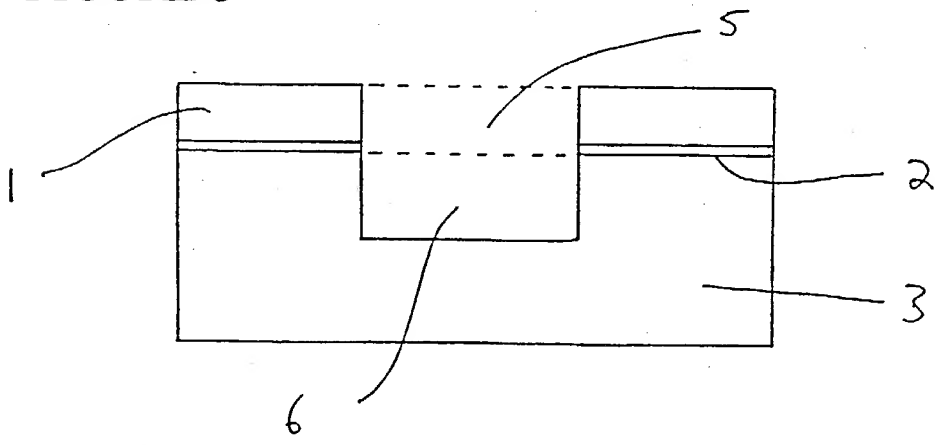

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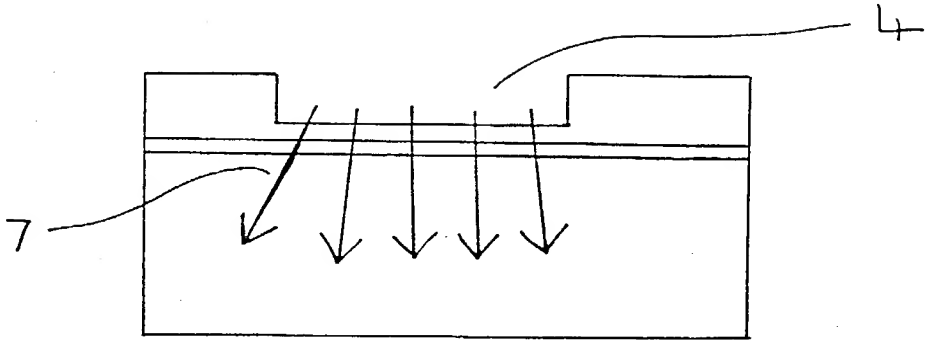

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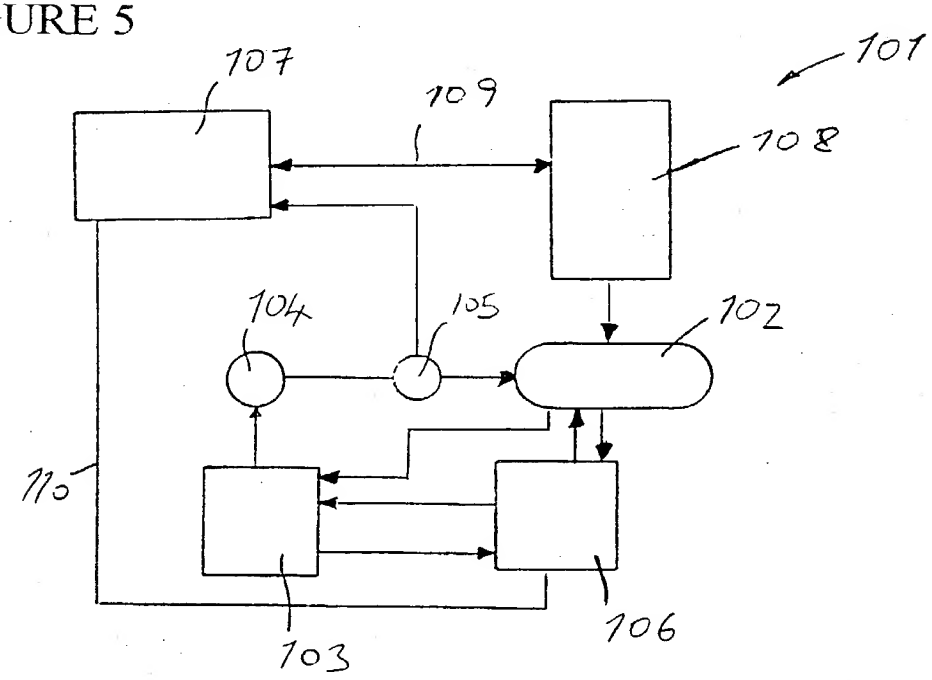

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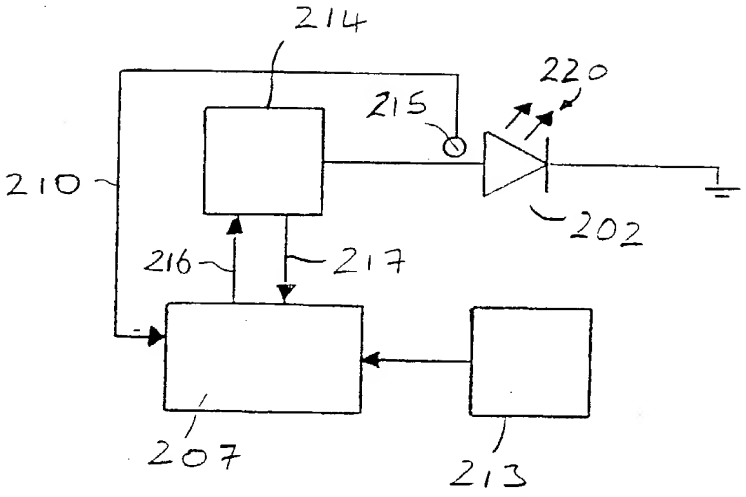
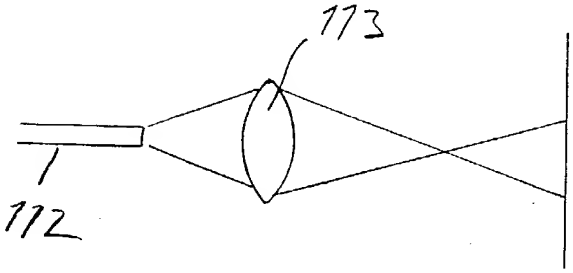


FIGURE 7



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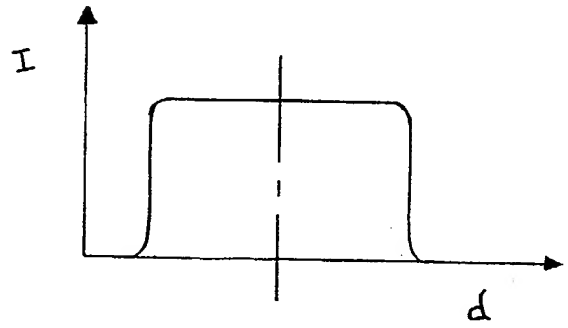

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Practitioner's Docket No. 698.22-US1 PATENT

COMBINED DECLARATION AND POWER OF ATTORNEY

(ORIGINAL, DESIGN, NATIONAL STAGE OF PCT, SUPPLEMENTAL, DIVISIONAL, CONTINUATION, OR C-I-P)

As a below named inventor, I hereby declare that:

TYPE OF DECLARATION

This declaration is for a national stage of PCT application.

INVENTORSHIP IDENTIFICATION

My residence, post office address and citizenship are as stated below, next to my name. I believe that I am an original, first and joint inventor of the subject matter that is claimed, and for which a patent is sought on the invention entitled:

TITLE OF INVENTION

Skin Wrinkle Reduction Using Pulsed Light

SPECIFICATION IDENTIFICATION

The specification is attached hereto and is a 371 of PCT/GB00/00749 which claims priority to GB 9905173.2.

ACKNOWLEDGMENT OF REVIEW OF PAPERS AND DUTY OF CANDOR

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information, which is material to patentability as defined in 37, Code of Federal Regulations, Section 1.56.

PRIORITY CLAIM (35 U.S.C. Section 119(a)-(d))

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119(a)-(d) of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating

at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed.

Such applications have been filed as follows.

PRIOR PCT APPLICATION(S) FILED WITHIN 12 MONTHS (6 MONTHS FOR DESIGN) PRIOR TO THIS APPLICATION AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. SECTION 119(a)-(d)

INDICATE IF PCT	APPLICATION NUMBER	DATE OF FILING DAY, MONTH, YEAR	PRIORITY CLAIMED UNDER 35 U.S.C. SECTION 119
PCT	PCT/GB00/00749	3 March 2000	yes

ALL FOREIGN APPLICATION(S), *IF ANY*, FILED MORE THAN 12 MONTHS (6 MONTHS FOR DESIGN) PRIOR TO THIS U.S. APPLICATION

COUNTRY	APPLICATION NUMBER	DATE OF FILING DAY, MONTH, YEAR	PRIORITY CLAIMED UNDER 35 U.S.C. SECTION 119
UK	GB 9905173.2	5 March 1999	yes

POWER OF ATTORNEY

I hereby appoint the following practitioner(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

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David J. Zoetewey	45,258
Sandra Poteat Thompson	46,264
Martin Fessenmaier	46,697

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DECLARATION

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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